

# A *de novo* synthetic method to the access of *N*-substituted benzazepines

Lamiaa Ouchakour,<sup>a,b</sup> Melinda Nonn,<sup>a,b,d</sup> Matthias D'hooghe,<sup>c</sup> Loránd Kiss<sup>a,b\*</sup>

<sup>a</sup>*Institute of Pharmaceutical Chemistry, University of Szeged, H-6720 Szeged, Eötvös u. 6, Hungary*

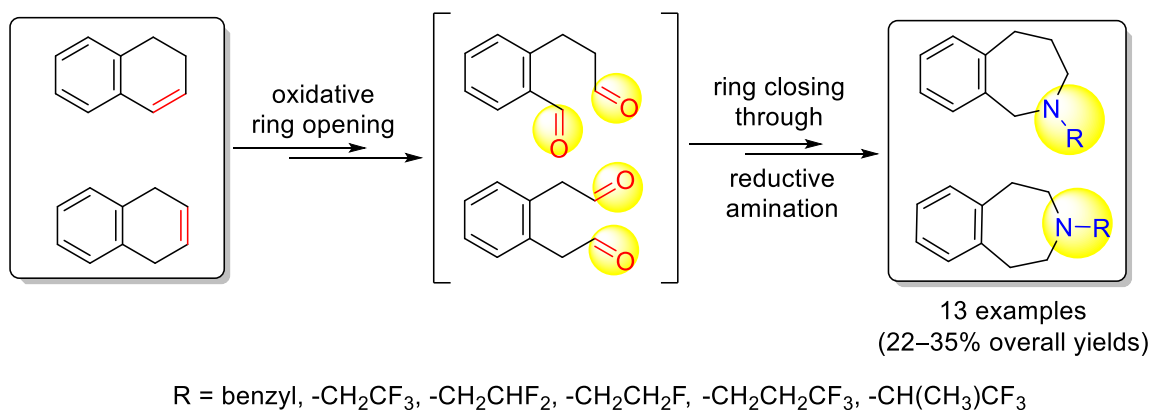
<sup>b</sup>*Interdisciplinary Excellence Centre, Institute of Pharmaceutical Chemistry, University of Szeged, H-6720 Szeged, Eötvös u. 6, Hungary*

<sup>c</sup>*Department of Green Organic Chemistry and Technology, Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, B-9000 Ghent, Belgium*

<sup>d</sup>*MTA-SZTE Stereochemistry Research Group, Hungarian Academy of Sciences, H-6720 Szeged, Eötvös u. 6, Hungary*

E-mail: [kiss.lorand@pharm.u-szeged.hu](mailto:kiss.lorand@pharm.u-szeged.hu)

**Abstract:** A novel, convenient procedure has been described for the construction of fluorine-containing benzazepines. The synthetic protocol starting from readily available dihydronaphthalene regioisomers is based on oxidative ring olefin bond cleavage followed by ring closure of the diformyl intermediates in the presence of some fluorine-containing primary amines across double reductive amination. The applicability of the developed synthetic method was demonstrated by the **Graphical abstract:**



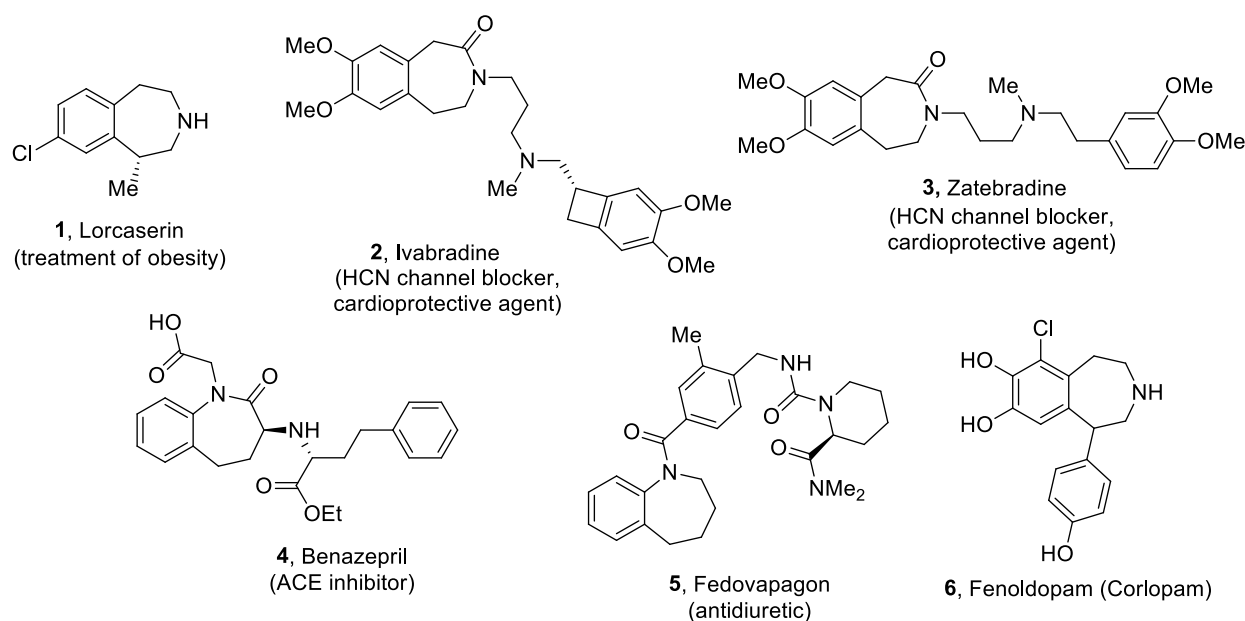
synthesis of 13 benzazepine compounds isolated in 22–35% overall yields.

**Keywords:** benzazepine, fluorine, reductive amination, ring expansion, azaheterocycle, ring closing

## Introduction

Functionalized azepanes constitute important components of several biologically relevant natural and non-natural products with interesting pharmaceutical properties. Some representatives of this class of azaheterocycles are known as antiviral agents, glycosidase inhibitors, anticancer agents or antidiabetics [1-5]. Therefore, in view of their medicinal relevance, an increasing number of synthetic methods have been described in recent years for the construction of highly substituted azepane derivatives [6-10]. Fluorine chemistry has become a rapidly expanding research area during the last 10–15 years. Because of the high impact of organofluorine molecules in drug research (approximately 25% of the drugs introduced in the market contain at least one fluorine atom) and agrochemistry, the synthesis of fluorinated organic scaffolds has been recognized to be a hot topic in synthetic organic chemistry over the past decades [11-13]. This high interest is based on the general understanding that the presence of fluorine atom(s) can influence biological property, metabolic stability, acid–base character, and lipophilicity [14-20]. Functionalized azepanes are important frameworks in small drug molecular design. Accordingly, the incorporation of F atom(s) in these seven-membered azaheterocycles has generated increasing interest in pharmaceutical research.

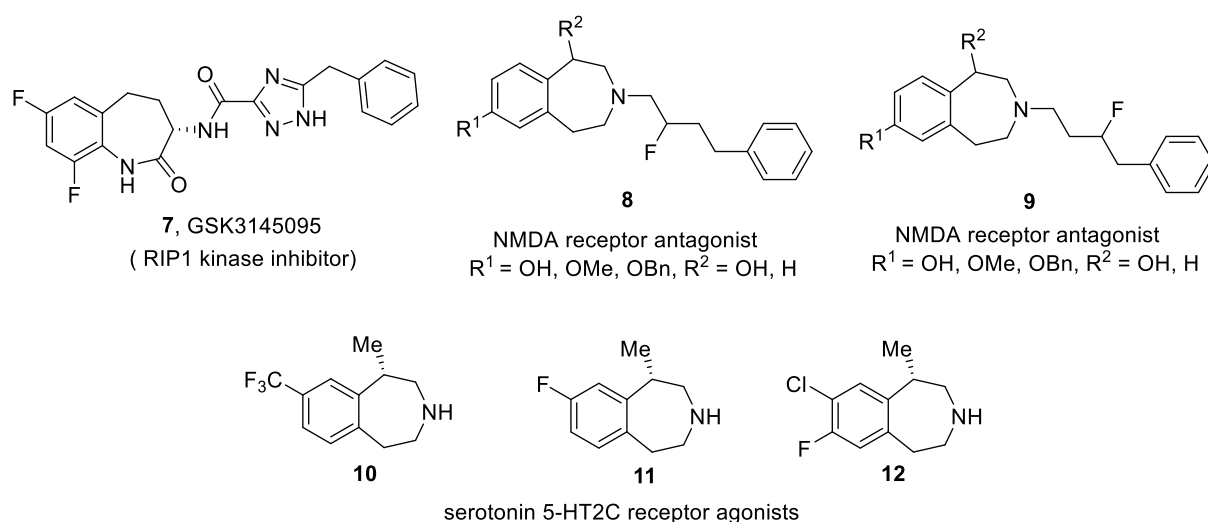
Benzo-fused azepines (benzazepines) including their functionalized derivatives form a relevant subclass in the area of azaheterocyclic compounds. Many representatives of these compounds, some of them found in various commercial drugs, are known to possess important biological properties. The structures of some representative drugs with a benzazepine core are presented on Figure 1.



**Figure 1.** Structures of some bioactive benzazepine derivatives.

For example, Lorcaserin (**1**) [21] is a drug used in the treatment of obesity, Ivabradine (**2**) [15] and Zatebradine (**3**) [22] are cardioprotective drugs (hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker), Benazepril (**4**) [23] is known as angiotensin-converting enzyme (ACE) inhibitor, Fedovapagon (**5**) [23] possesses antidiuretic properties, while Fenoldopam (Corlopam) (**6**) [24] is a D1-like receptor agonist (Figure 1).

Despite the fact that a relatively large number of functionalized azepanes, fluorine-containing azepines, and various benzazepines with biological properties are known, there are only a very limited number of examples of fluorine-containing bioactive benzazepines available in the literature. The structure of several representatives of this group of bioactive products is collected in Figure 2 (structures **7–12**) [25-27].



**Figure 2.** Several fluorine-containing benzazepines with biological activities.

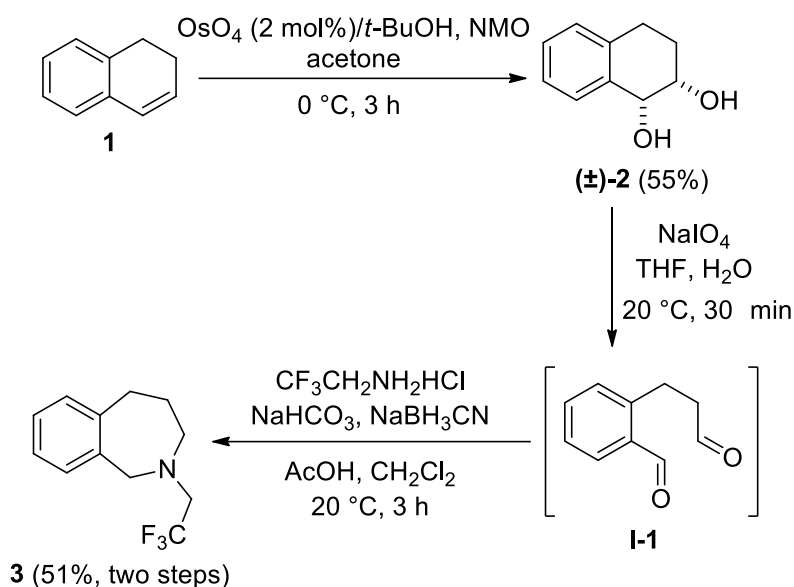
Considering the potential biological importance of fluorine-containing benzazepines on the one hand and the limited number of literature reports on these scaffolds on the other hand, the development of new synthetic strategies towards these structures represents a relevant challenge in synthetic organic chemistry. Within that framework, the main objective of this research involved the preparation of different types of fluorine-containing benzazepines via a convenient new approach.

## Results and Discussion

The synthetic concept towards the construction of benzazepine scaffolds was based on our earlier findings regarding the synthesis of functionalized, saturated azaheterocyclic substances. This protocol involved the oxidative cleavage of the ring olefin bond of substituted cycloalkenes, followed by ring closing of the diformyl intermediates mediated by double reductive amination with various primary amines [28-30].

Our synthetic strategy for the creation of the benzazepine ring system started with the dihydroxylation of the ring C–C double bond of 1,2-dihydronaphthalene (**1**) with OsO<sub>4</sub> (2 mol%)/NMO in acetone at room temperature, which provided the corresponding *cis*-diol derivative (**±**)-**2** [31]. Vicinal diol (**±**)-**2** was next subjected to oxidative C–C ring cleavage with NaIO<sub>4</sub> in a THF/H<sub>2</sub>O solvent system giving an unstable diformyl intermediate (**I-1**), which was then used further without isolation. It is well known that fluorine atoms incorporated into the structure of an organic scaffold, especially in the skeleton of an azaheterocycles, will significantly affect basic characteristics. Therefore, we intended to carry out the construction of the benzazepine skeleton by ring closing of dialdehyde intermediate **I-1** using various

fluorine-containing primary amines. First we selected trifluoroethylamine as the amine component.

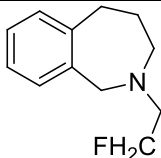
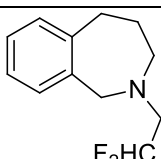
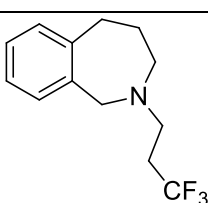
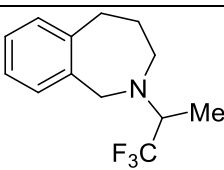
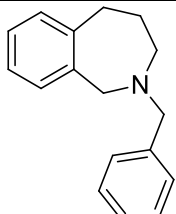
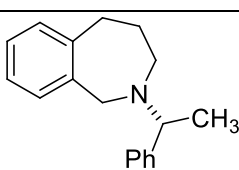


**Scheme 1.** Synthesis of benzazepine **3** containing a trifluoromethyl group.

Thus, dialdehyde **I-1** resulting from the ring opening of diol ( $\pm$ )-**2** was submitted to double reductive amination with 2,2,2-trifluoroethylamine hydrochloride in the presence of  $\text{NaHCO}_3$  and reducing agent in  $\text{CH}_2\text{Cl}_2$  at room temperature. After investigating various reducing agents such as  $\text{NaBH}_4$ ,  $\text{NaBH}(\text{OAc})_3$  and  $\text{NaBH}_3\text{CN}$ , while the first two provided the desired product in low yields (12% and 18%), the reaction in the presence of the latter reagent, after 3 h, yielded the corresponding trifluoromethyl-containing benzazepine **3** in moderate yield (55%, two steps) (Scheme 1) confirming the feasibility of the proposed synthetic strategy.

In continuation, we extended the protocol described above towards the preparation of other benzazepines derivatives. Thus, diol ( $\pm$ )-**2** was submitted to  $\text{NaIO}_4$ -mediated ring opening followed by subsequent treatment of diformyl intermediate **I-1** with four different fluorine-containing primary amines: 2-fluoroethylamine, 2,2-difluoroethylamine, 3,3,3-trifluoropropylamine, and 1,1,1-trifluoropropan-2-amine. The reductive amination with the involvement of cyclization provided the corresponding fluorine-containing benzazepines **4–7** (Table 1).

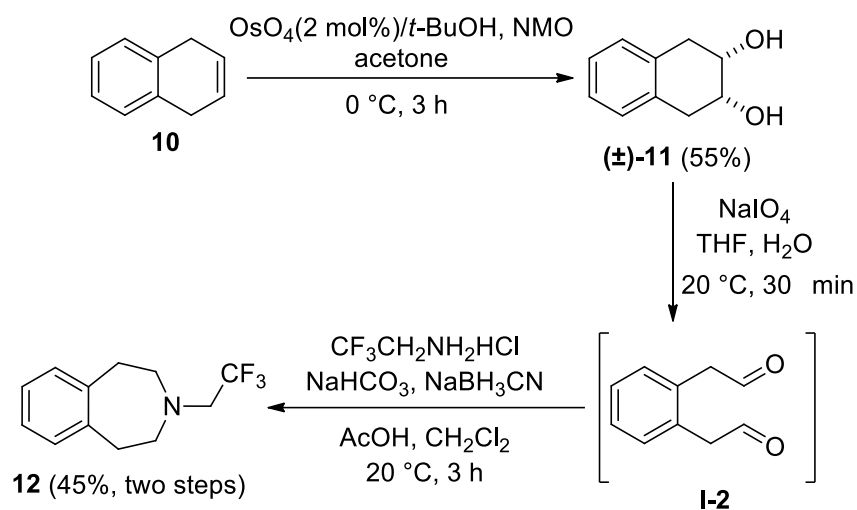
fluorine-containing amine	product	yield (two steps); compound number
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$\text{H}_2\text{N}-\text{CH}_2\text{CH}_2\text{F}$		45%, ( <b>4</b> )
$\text{H}_2\text{N}-\text{CH}(\text{F})_2$		26%, ( <b>5</b> )
$\text{H}_2\text{N}-\text{CH}_2\text{CH}_2\text{CF}_3$		25%, ( <b>6</b> )
$\text{H}_2\text{N}-\text{CH}(\text{Me})\text{CF}_3$		43%, ( <b>7</b> )
$\text{H}_2\text{N}-\text{CH}_2\text{C}_6\text{H}_5$		55%, ( <b>8</b> )
$\text{Ph}-\text{CH}(\text{Me})\text{NH}_2$		47%, ( <b>9</b> )

**Table 1.** Synthesized benzazepane derivatives **4–9** from diol ( $\pm$ )-**2**.

Obviously, this procedure could be applied for the access of non-fluorinated derivatives as well. When benzylamine or (*R*)-methylbenzylamine its methyl-substituted counterpart was reacted, the corresponding benzazepines **8** and **9** could be isolated in moderate yields (two steps, 47% and 55%) (Table 1).

Next, we intended to further extend the synthetic methodology and increase the number of benzazepine derivatives by targeting structural isomers. Accordingly, 1,4-dihydronaphthalene (**10**) a regioisomer of **1** was subjected to the same oxidative ring opening. First compound **10** under OsO<sub>4</sub>-mediated dihydroxylation conditions yielded the corresponding diol ( $\pm$ )-**11**,<sup>8</sup> which subsequently underwent ring opening upon treatment with NaIO<sub>4</sub> to furnish diformyl intermediate **I-2** (Scheme 2).



**Scheme 2.** Synthesis of benzazepine **12** containing a trifluoromethyl group.

fluorine-containing amine	product	yield (two steps); compound number
$\text{H}_2\text{NCH}_2\text{CH}_2\text{F}$		25%, ( <b>13</b> )
$\text{H}_2\text{NCH}_2\text{CHF}_2$		26%, ( <b>14</b> )
$\text{H}_2\text{NCH}_2\text{CH}_2\text{CF}_3$		36%, ( <b>15</b> )
		30%, ( <b>16</b> )
		58%, ( <b>17</b> )

**Table 2.** Synthesized benzazepane derivatives **13–17** diol (±)-**11**.

Similar to Scheme 1, dialdehyde **I-2** was used in the forthcoming step without isolation. Thus on treatment with 2,2,2-trifluoroethylamine in the presence of  $\text{NaBH}_3\text{CN}$ , double

reductive amination afforded by cyclization the desired benzazepine derivative **12** containing the trifluoromethyl group. This product is a regioisomer of **3** (45%, two steps) (Scheme 2).

Finally, diformyl intermediate **I-2** derived from diol **11** was treated with the fluorinated primary amines 2-fluoroethylamine, 2,2-difluoroethylamine, 3,3,3-trifluoropropylamine, 1,1,1-trifluoropropan-2-amine and benzylamine under reductive condition, in the presence of NaBH<sub>3</sub>CN, to deliver the corresponding opposite regioisomers **13–17** in moderate yield (Scheme 2).

## Conclusions

In this paper we described a novel route for the construction of 2-benzazepine and 3-benzazepine ring systems starting from dihydronaphthalene regioisomers, providing a convenient access to both tetrahydrobenzo[*c*]azepine and tetrahydrobenzo[*d*]azepine regioisomers. The key steps of the synthetic procedure are (i) oxidative olefin bond cleavage of dihydronaphthalenes followed by (ii) cyclization resulting in a formal ring expansion under reductive amination with various primary amines. In view of the importance of organofluorine scaffolds, we applied fluorinated amines for the ring-closing step, which yielded various fluorine-containing benzazepines. Further extensions of the described procedure regarding the access of functionalized benzazepines are currently being studied in our laboratory.

## Experimental

### General procedure for dihydroxylation of dihydronaphthalene

To a solution of 1,2-dihydronaphthalene or 1,4-dihydronaphthalene (2 mmol) in acetone (30 mL) was added NMO (1.5 equiv) at 0 °C with stirring, followed by addition of a solution of 2% OsO<sub>4</sub> in *t*-butyl alcohol (0.3 mL). Next the resulting mixture was stirred for 3 h at room temperature. After termination of the reaction (monitored by TLC) 10 mL of saturated aqueous Na<sub>2</sub>SO<sub>3</sub> solution was added and the reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated under reduced pressure. The crude product was purified by means of column chromatography on silica gel (*n*-hexane/EtOAc or *n*-hexane/acetone).

### General procedure for the synthesis of fluorine-containing benzazepine derivative by oxidative ring cleavage followed by ring closure by reductive amination

To a stirred solution of dihydroxylated tetrahydronaphthalene (2 mmol) NaIO<sub>4</sub> (1.5 equiv) was added in THF/H<sub>2</sub>O (25 mL/2 mL). After stirring for 30 min at 20 °C under Ar atmosphere, H<sub>2</sub>O



was added (40 mL). The mixture was then extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL) and the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. The resulting solution containing the dialdehyde derivative concentrated to half of its volume was used without purification for the next reaction. To the solution of the dialdehyde was added fluorine-containing amine hydrochloride (1 equiv) and NaHCO<sub>3</sub> (2 equiv) or benzylamine or methylbenzylamine (1 equiv, without NaHCO<sub>3</sub>). Then the mixture was stirred at 20 °C for 10 min and, after adding NaBH<sub>3</sub>CN (1 equiv) and AcOH (2 drops), stirring was continued for another 3 h at 20 °C. The reaction mixture was diluted with H<sub>2</sub>O (20 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc or *n*-hexane/acetone).

*Characterization and <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of the synthesized compounds are available in the Supporting Information*

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## References

- [1] A. Barbero, A. Diez-Varga, F. J. Pulido, A. González-Ortega, Synthesis of Azepane Derivatives by Silyl-aza-Prins Cyclization of Allylsilyl Amines: Influence of the Catalyst in the Outcome of the Reaction, *Org. Lett.* 18 (2016) 1972–1975.
- [2] E. Cini, G. Bifulco, G. Menchi, M. Rodriguez, M. Taddei, ChemInform Abstract: Synthesis of Enantiopure 7-Substituted Azepane-2-carboxylic Acids as Templates for Conformationally Constrained Peptidomimetics, *Eur. J. Org. Chem.* (2012) 2133–2141.
- [3] A. Hameed, S. Javed, R. Noreen, T. Huma, S. Iqbal, H. Umbreen, T. Gulzar, T. Farooq, Facile and Green Synthesis of Saturated Cyclic Amines, *Molecules* 22 (2017) 1691/1–1691/22.
- [4] A. Nortcliffe, C. J. Moody, Seven-membered ring scaffolds for drug discovery: Access to functionalised azepanes and oxepanes through diazocarbonyl chemistry, *Bioorg. Med. Chem.* 23 (2015) 2730–2735.

- [5] D. G. Wishka, M. Bédard, K. E. Brighty, R. A. Buzon, K. A. Farley, M. W. Fichtner, G. S. Kauffman, J. Kooistra, J. G. Lewis, H. O'Dowd, I. J. Samardjiev, B. Samas, G. Yalamanchi, M. C. Noe, An asymmetric synthesis of (2S,5S)-5-substituted azepane-2-carboxylate derivatives, *J. Org. Chem.* 76 (2011) 1937–1940.
- [6] O. René, I. A. Stepek, A. Gobbi, B. P. Fauber, S. Gaines, Palladium-Catalyzed Ring Expansion of Spirocyclopropanes to Form Caprolactams and Azepanes, *J. Org. Chem.* 80 (2015) 10218–10225.
- [7] B. Drouillat, I. V. Dorogan, M. Kletsii, O. N. Burov, F. Couty, Competitive Ring Expansion of Azetidines into Pyrrolidines and/or Azepanes, *J. Org. Chem.* 81 (2016) 6677–6685.
- [8] J. Choi, N. N. Yadav, H. J. Ha, Preparation of a Stable Bicyclic Aziridinium Ion and Its Ring Expansion toward Piperidines and Azepanes, *Asian J. Org. Chem.* 6 (2017) 1292–1307.
- [9] D. V. Yarmoliuk, D. Serhiichuk, V. Smyrnov, A. V. Tymtsunik, O. V. Hryshchuk, Y. Kuchkovska, O. O. Grygorenko, Synthesis of azabicyclo[n.1.0]alkane-derived bifunctional building blocks via the Corey–Chaykovsky cyclopropanation, *Tetrahedron Lett.* 59 (2018) 4611–4615.
- [10] J. Zhou, Y. Y. Yeung, N-Bromosuccinimide-Induced Aminocyclization–Aziridine Ring-Expansion Cascade: An Asymmetric and Highly Stereoselective Approach toward the Synthesis of Azepane, *Org. Lett.* 16 (2014) 2134–2137.
- [11] J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok, H. Liu, Fluorine in pharmaceutical industry: fluorine-containing drugs introduced to the market in the last decade (2001-2011), *Chem. Rev.* 114 (2014) 2432-2506.
- [12] Fluorine in Pharmaceutical and Medicinal Chemistry: From Biophysical Aspects to Clinical Applications, Imperial College Press, London (2012). Edited by Gouverneur, V. and Müller, K..
- [13] Y. Zhou, Y. Wang, Z. Gu, S. Wang, W. Zhu, J. L. Acena, V. A. Soloshonok, K. Izawa, H. Liu, Next Generation of Fluorine-Containing Pharmaceuticals, Compounds Currently in Phase II–III Clinical Trials of Major Pharmaceutical Companies: New Structural Trends and Therapeutic Areas, *Chem. Rev.* 116 (2016) 442-518.
- [14] C. Chen, P. Kattanguru, O. A. Tomashenko, R. Karpowicz, G. Siemiaszko, A. Bhattacharya, V. Calasans, Y. Six, Synthesis of functionalised azepanes and piperidines from bicyclic halogenated aminocyclopropane derivatives, *Org. Biomol. Chem.* 15 (2017) 5364–5372.

- [15] S. Fustero, F. Mojarrad, M. D. P. Carrión, J. F. Sanz-Cervera, J. L. Aceña, Organocatalytic anti-Selective Mannich Reactions with Fluorinated Aldimines: Synthesis of anti- $\gamma$ -Fluoroalkyl- $\gamma$ -amino Alcohols, *Eur. J. Org. Chem.* (2009) 5208–5214.
- [16] G. Masson, S. Riota, D. G. Pardo, J. Cossy, Access to Enantio-enriched Substituted  $\alpha$ -Trifluoromethyl Azepanes from l-Proline, *Org. Lett.* 20 (2018) 5019–5022.
- [17] S. N. Osipov, O. I. Artyushin, A. F. Kolomiets, C. Bruneau, M. Picquet, P. H. Dixneuf, Synthesis of Fluorine-Containing Cyclic  $\alpha$ -Amino Acid and  $\alpha$ -Amino Phosphonate Derivatives by Alkene Metathesis, *Eur. J. Org. Chem.* (2001) 3891–3897.
- [18] O. I. Shmatova, N. E. Shevchenko, E. S. Balenkova, G. V. Rösenthaller, V. G. Nenajdenko, Highly  $\beta$ -Regioselective Friedel–Crafts Aminoalkylation of Pyrroles with Cyclic Perfluoroalkylated Imines, *Eur. J. Org. Chem.* (2013) 3049–3058.
- [19] N. F. Shevchenko, K. Vlasov, V. G. Nenajdenko, G. V. Rösenthaller, The reaction of cyclic imines with the Ruppert–Prakash reagent. Facile approach to  $\alpha$ -trifluoromethylated nornicotine, anabazine, and homoanabazine, *Tetrahedron* 67 (2011) 69–74.
- [20] W. B. Zhao, S. Nakagawa, A. Kato, I. Adachi, Y. M. Jia, X. G. Hu, G. W. J. Fleet, F. X. Wilson, G. Horne, A. Yoshihara, K. Izumori, C. Y. Yu, General Synthesis of Sugar-derived Azepane Nitrones: Precursors of Azepane Iminosugars, *J. Org. Chem.* 78 (2013) 3208–3221.
- [21] A. Cabré, X. Verdager, A. Riera, Enantioselective Synthesis of  $\beta$ -Methyl Amines via Iridium-Catalyzed Asymmetric Hydrogenation of N-Sulfonyl Allyl Amines, *Adv. Synth. Catal.* 361 (2019) 4196–4200.
- [22] M. N. Romanelli, M. D. Lungo, L. Guandalini, M. Zobeiri, A. Gyökeres, T. Árpádfy-Lovas, I. Koncz, L. Sartiani, G. Bartolucci, S. Dei, D. Manetti, E. Teodori, T. Budde, E. Cerbai, EC18 as a Tool To Understand the Role of HCN<sub>4</sub> Channels in Mediating Hyperpolarization-Activated Current in Tissues, *ACS Med. Chem. Lett.* 10 (2019) 584–589.
- [23] R. Wang, R. X. Jin, Z.Y. Qin, K. J. Bian, X. S. Wang, Novel and facile synthesis of 1-benzazepines via copper-catalyzed oxidative C(sp<sup>3</sup>)-H/C(sp<sup>2</sup>)-H cross-coupling, *Chem. Commun.* 53 (2017) 12229–12232.
- [24] H. J. Böhm, A. Flohr, M. Stahl, Scaffold hopping, *Drug Discov. Today: Technologies* 1 (2004) 217–224.
- [25] P. A. Harris, J. M. Marinis, J. D. Lich, S. B. Berger, A. Chirala, J. A. Cox, P. M. Eidam, J. N. Finger, P. J. Gough, J. U. Jeong, J. Kang, V. Kasparcova, L. K. Leister, M. K. Mahajan, G. Miller, R. Nagilla, M. T. Ouellette, M. A. Reilly, A. R. Rendina, E. J. Rivera, H. H. Sun, J. H. Thorpe, R. D. Totoritis, W. Wang, D. Wu, D. Zhang, J. Bertin, R. W. Marquis,

- Identification of a RIP1 Kinase Inhibitor Clinical Candidate (GSK3145095) for the Treatment of Pancreatic Cancer, *ACS Med. Chem. Lett.* 10 (2019) 857-862.
- [26] B. M. Smith, J. M. Smith, J. H. Tsai, J. A. Schultz, C. A. Gilson, S. A. Estrada, R. R. Chen, D. M. Park, E. B. Prieto, C. S. Gallardo, D. Sengupta, P. I. Dosa, J. A. Covel, A. Ren, R. R. Webb, N. R. A. Beeley, M. Martin, M. Morgan, S. Espitia, H. R. Saldana, C. Bjennig, K. T. Whelan, A. J. Grottick, F. Menzaghi, W. J. Thomsen, Discovery and Structure-Activity Relationship of (1R)-8-Chloro-2,3,4,5-tetrahydro-1-methyl-1H-3-benzazepine (Lorcaserin), a Selective Serotonin 5-HT<sub>2C</sub> Receptor Agonist for the Treatment of Obesity *J. Med. Chem.* 51 (2008) 305–313.
- [27] S. Thum, D. Schepmann, E. Ayet, M. Pujol, F. R. Nietoc, S. M. Ametamey, B. Wünsch, Tetrahydro-3-benzazepines with fluorinated side chains as NMDA and  $\sigma$ <sub>1</sub> receptor antagonists: Synthesis, receptor affinity, selectivity and antiallodynic activity *Eur. J. Med. Chem.* 177 (2019) 47-62.
- [28] L. Ouchakour, R. A. ÁbrahÁmi, E. Forró, M. Haukka, F. Fülöp, L. Kiss, Stereocontrolled Synthesis of Fluorine-Containing Piperidine  $\gamma$ -Amino Acid Derivatives, A De Novo Synthetic Route to 1,2,3,4-Tetrahydroisoquinoline Derivatives, *Eur. J. Org. Chem.* (2019) 2202–2211.
- [29] R. A. ÁbrahÁmi, S. Fustero, F. Fülöp, L. Kiss, *Synlett* 29 (2018) 2066–2070.
- [30] R. A. ÁbrahÁmi, L. Kiss, S. Fustero, F. Fülöp, Functionalized Dialdehydes as Promising Scaffolds for Access to Heterocycles and  $\beta$ -Amino Acids: Synthesis of Fluorinated Piperidine and Azepane Derivatives, *Synthesis* 49 (2017) 1206–1213.
- [31] D. Dalmizrak, H. Göksu, M. S. Gültekin, A facile synthesis of vicinal cis-diols from olefins catalyzed by in situ generated Mn<sub>x</sub>O<sub>y</sub> nanoaggregates, *RSC Advances* 5 (2015) 20751-20755.